Epidemiological analysis of viral infections as risk factors for multiple sclerosis

Akademisk avhandling

som för avläggande av medicine doktorsexamen
vid Sahlgrenska Akademin vid Göteborgs universitet
kommer att offentligen försvaras i hörsal Arvid Carlsson,
Academicum, Medicinaregatan 3
Fredagen den 5 juni 2009 kl 13:00

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Based on the following papers

I Ahlgren C, Taranger J, Johansson L, Andersen O. Elimination of childhood diseases: possible influence on the incidence of multiple sclerosis soon detectable. Neuroepidemiology. 2002;21(6):306-9.

II Ahlgren C, Andersen O. No major birth order effect on the risk of multiple sclerosis. Neuroepidemiology. 2005;24(1-2):38-41.

III Ahlgren C, Oden A, Toren K, Andersen O. Multiple sclerosis incidence in the era of measles-mumps-rubella mass vaccinations. Acta Neurol Scand. 2009;119(5):313-20.

IV Ahlgren C, Oden A, Toren K, Andersen O. A population-based case-control study on viral infections and vaccinations and subsequent MS risk. Manuscript – Submitted

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Epidemiological analysis of viral infections as risk factors for multiple sclerosis

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Viral childhood diseases have been implicated in the pathogenesis of multiple sclerosis (MS). Swedish mass vaccination programmes resulted in radical changes in the panorama of the targeted infections. Vaccines against measles, mumps and rubella were implemented in the early 1970s. In 1982, Sweden introduced the two-dose measles-mumps-rubella (MMR) vaccine, as the first country in the world. Measles sharply declined in the 1970s. In cohorts born since 1981, measles, mumps and rubella were virtually eliminated. The main aim of this thesis was to investigate whether specific viral childhood diseases, or the vaccinations against them, influence the risk of developing MS. This was accomplished by a study of MS incidence in vaccinated cohorts, by a case-control study and – indirectly – by a study of birth order in sibships.

These studies were based on unique underlying conditions. Individual data on infections and vaccinations were documented in child health and school health records. The proportion of individuals with a history of vaccination-targeted infections was suitable for statistical analyses. Furthermore, there was a long tradition of MS incidence studies in Gothenburg. We updated the Gothenburg MS registry obtaining a study material of 534 incident MS patients born from 1959 to 1990. The incidence of MS was analysed in four population cohorts, each selected to represent a new vaccination programme. Questionnaires on measles, mumps, rubella, or the vaccinations, and two other infections, varicella and infectious mononucleosis were completed by 509 MS patients and 2067 controls, born 1959 to 1986. Data on infections and vaccinations were obtained from the questionnaires and, for a selection of 206 MS patients and 888 controls, also from child health and school health records.

We found no major influence of birth order on MS risk. The observed number of first-born patients did not significantly differ from the expected number, and the proportion of first-borns did not differ from that in a control cohort born during the same period. We found no significant change in the incidence of MS in any of the four population cohorts defined by mass vaccinations. The long-term MS incidence showed a significant gradual age-dependent increase, which was unrelated to the introduction of the vaccination programmes. MS patients and controls reported similar frequencies of measles, mumps, rubella and varicella. The results from the child health and school health records confirmed the results from the questionnaires. Infectious mononucleosis was associated with 2-fold higher MS risk. In the light of this positive finding, the negative findings for the other studied infections are more convincing. Simply being vaccinated against measles, mumps or rubella did not change the risk of MS. Similarly, MMR vaccinated individuals were not at higher or lower MS risk than MMR unvaccinated individuals. Among MMR vaccinated individuals, the MS risk was increased in those vaccinated before age 10 only. Those vaccinated both before and after age 10 had intermediate MS risk.

The specific viral childhood diseases measles, mumps, rubella and varicella do not influence the risk of MS, and may be dismissed as risk factors for MS. Infectious mononucleosis is a moderate risk factor for MS. Vaccination against Epstein-Barr virus infection should be considered. The risk of MS in MMR vaccinated does not differ from that in MMR unvaccinated individuals. The finding that MMR vaccination at a low age only may be related to MS risk needs to be confirmed in other study material.

ISBN-978-91-628-7809-2 Göteborg 2009